C7

22. (Amended) The method of Claim 21, wherein said administering is by injection.

23. (Amended) The method of Claim 21, wherein said site is a tumor.

N.E.

24. The method of Claim 9, wherein said individual is in need of inhibition of cell proliferation, and wherein said administering is locally to a site wherein cell proliferation is to be inhibited.

25. The method of Claim 24, wherein said administering is by injection.

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26. (Amended) The method of Claim 24, wherein said site is a tumor.

27. (Amended) The method of Claim 11, wherein said site is a tumor or where a tumor was previously located prior to removal.

N.E

28. The method of Claim 11, wherein said administering is by injection to a tumor

REMARKS

Claims 1-6 and 8-28 are pending in the instant application. Claim 14 is canceled by this amendment. Claims 1-16, 9-14, 12, 20, 23, 26 and 27 stand objected to for minor informalities. Claims 1-6 and 8-28 stand rejected under 35 U.S.C. § 112. Claim 14 stands rejected under 35 U.S.C. § 102(b). Claims 1, 2, 4, 5, 8-12, and 14-28 stand rejected under 35 U.S.C. § 102(a). A page entitled "Version Showing Changes Made" is attached which shows the amendments presented in this response. In addition, an Appendix of Pending Claims, which reflect the claims after entry of this amendment, is attached for the Examiner's convenience.

Drawings

The drawings stand objected to, and the Examiner has required corrected drawings. As corrected drawings are included with this amendment, Applicants respectfully request withdrawal of the objection.

Claim Objections

Claims 1-6 and 9-14 stand objected to for lack of uniformity in the recitation of "RAD51." As all remaining claims now recite "RAD51" in all capital letters, Applicants respectfully request withdrawal of this objection.

Claims 17, 20, 23, 26 and 27 stand objected to for grammatical inconsistency. As shown in the amended claim set above, these claims are now grammatically consistent. Accordingly, Applicants respectfully request withdrawal of this objection.

35 U.S.C. § 112

Claims 1-6 and 8-28 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Specifically, the Examiner asserts that the claims are drawn to various methods utilizing RAD51 antisense, but the claims do not have a final step stating that the claimed function has been achieved. As shown in the amended claim set above, the claims remaining after this amendment have been amended to include a recitation of the claimed function. Accordingly, Applicants respectfully request withdrawal of this rejection.

Claims 1-6 and 8-28 stand rejected under 30 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the application was filed, had possession of the claimed invention. In particular, the Examiner asserts that the specification does not provide support for RAD51 antisense sequences other than SEQ ID NOS: 1 and 2. Applicants respectfully disagree.

As quoted by the Examiner in her most recent Office Action, MPEP 2163 states, "the written description requirement for a claimed genus may be satisfied...by functional characteristics coupled with a known or disclosed correlation between function and structure..." In satisfaction of this requirement, the applicant has provided numerous target sequences for the production of specific antisense structures, (see the various citations on page 6, lines 13-25, all of which are incorporated by reference on page 11, lines 27-28). In addition, on page 5, lines 1-11, the antisense molecules are further detailed as having defined lengths and levels of complementarity with such targets. Finally, the applicant has provided examples of antisense molecules based on such a target structure that performs the claimed function. Accordingly, the applicant has provided a *functional characteristic* (RAD51 activity modulation in a cell) *and disclosed a correlation between that function and structure* (providing a functional antisense oligonucleotide and the structures of target sequences which can be used as the basis of other antisense oligonucleotides). Therefore the written description of the claimed genus is satisfied and withdrawal of the rejection of the remaining claims is respectfully requested.

Claims 1-6, 8-13, and 15-28 stand rejected under 35 U.S.C. § 112, first paragraph, as the Examiner asserts that the specification does not provide enablement for any method of administration and treatment of any whole organism as broadly claimed. Specifically, the Examiner maintains that there is insufficient teaching regarding the effective delivery of antisense molecules to the whole organism while specifically targeting certain tissues; regarding stability of the antisense molecule in vivo; and regarding dosage and toxicity. Applicants respectfully disagree.

The test of enablement is whether one of ordinary skill in the art would be able to make and use the claimed invention without undue experimentation, based on the disclosure and the prevailing knowledge in the field (*see* MPEP § 2164.01). Applicants submit that the present claims are enabled based on the data provided in the specification, and published reports of similar work.

The Examiner first argues that no guidance has been provided in the art or the instant specification as to how RAD51 antisense may be delivered to a representative number of cells or tissues and therefore one of skill in the art would necessarily have to resort to undue experimentation to administer the claimed invention. On the contrary, the instant application and the knowledge in the art at the time the application was filed provide extensive guidance to the skilled practitioner in devising a method of delivery. Examples of methods not requiring direct injection into tumor cells (direct injection methods being described is in the instant application at pages 12-17) include the following; Lee et al. (Ann. Thorac. Surg. 66(3):903-907 (1998)) showed that intrajugular injection of a liposome suspension of nucleic acids produced strong expression in the heart and lungs, with negligible expression in the liver and kidneys; Ma et al. (Blood 90(7):2738-2746 (1997)) reduced liver tumors arising from a metastatic intraocular tumor both by intraocular and intravenous injection of an adenoviral vector encoding plasminogen activator inhibitor type 1. Accordingly, one skilled in the art would not have to resort to undue experimentation to devise an administration methodology, but rather could design an administration methodology based on the successful methodologies known at the time the application was filed.

The Examiner also argues that there is a lack of predictability in extrapolating the effectiveness from one antisense molecule to another, particularly with regard to stability, dosage and toxicity. As discussed above, the instant specification and the cited art provide examples of the effective use of a diverse group of antisense oligonucleotides. These examples occur in both cultured cell lines and in living tissues. In light of these examples, it is respectfully submitted that stability, dosage and toxicity are not obstacles to the practice of the instant invention. Rather these issues have been, and therefore could also in the future be, resolved employing routine experimentation by one skilled in the art.

35 U.S.C. § 102(b)

Claim 14 stands rejected under 35 U.S.C. § 102(b) as anticipated by Taki et al., Biochem. Biophys. Res. Comm. 223:434-438, 1996. As Claim 14 is canceled, without prejudice to pursing the claimed subject matter in one or more related applications, by the present amendment, withdrawal of this rejection is respectfully requested.

35 U.S.C. § 102(a)

Claims 1, 2, 4, 5, 8-12, and 14-28 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Ohnishi et al., Biochem. Biophys. Res. Comm. 245:319-324, 1998. As the Ohnishi et al. reference is the Applicant's own work, it is not a proper 102(a) reference. Accordingly, withdrawal of this rejection is respectfully requested.

CONCLUSION

On the basis of the amendments and remarks presented herein, Applicants believe that this application is now in condition for immediate allowance. Applicants respectfully request that the Examiner pass this application to issue, and early notice of such is requested. This paper is filed under 37 C.F.R. section 1.34(a).

Respectfully submitted,
DORSEY & WHITNEY LLP

Date: 2/28/03

Richard F. Trecartin, Reg. No. 31,801

Four Embarcadero Center, Suite 3400
San Francisco, California 94111-4187
Telephone: (415) 781-1989
1105412

Version showing Changes Made

1. (Amended) A method for inhibiting cell proliferation in an individual in vivo comprising administering to said individual a composition comprising a RAD51 antisense molecule thereby inhibiting said cell proliferation.

2. (Amended) A method for inducing sensitivity to radiation in an individual in vivo comprising administering to said individual a composition comprising a RAD51 antisense molecule thereby inducing said sensitivity to radiation.

3. (Amended) A method for inducing sensitivity to a chemotherapeutic agent in an individual in vivo comprising administering to said individual a composition comprising a RAD51 antisense molecule thereby inducing said sensitivity to a chemotherapeutic agent.

4. (Amended) A method for inhibiting the growth of a cancerous cell comprising administering to said cell a composition comprising a RAD51 antisense molecule thereby inhibiting said growth of a cancerous cell.

5. (Amended) A method for inducing sensitivity to radiation in a cancerous cell comprising administering to said cell a composition comprising RAD51 antisense molecule thereby inducing said sensitivity to radiation.

6. (Amended) A method for inducing sensitivity to a chemotherapeutic agent in a cancerous cell comprising administering to said cell a composition comprising RAD51 antisense molecule thereby inducing said sensitivity to a chemotherapeutic agent.

8. The method of Claim 1 further comprising the step of administering radiation.

9. (Amended) A method of prolonging the survival of an individual comprising administration to said individual a [Rad51] RAD51 antisense molecule thereby prolonging said survival.

10. (Amended) A method of treating cancer in an individual comprising administration to said individual a [Rad51] RAD51 antisense molecule thereby treating said cancer in an individual.

11. (Amended) A method according to claim 10 wherein said administration comprises localized delivery of said [Rad51] RAD51 antisense molecule to a cancerous or potentially cancerous site.

12. (Amended) A method according to claim 11 wherein said method further comprises radiation treatment at said site.

13. (Amended) A method according to claim 11 wherein said method further comprises chemotherapeutic treatment of said patient.

15. The method of Claim 1, wherein said administering is locally to a site wherein said cell proliferation is to be inhibited.

16. The method of Claim 15, wherein said administering is by injection.

17. (Amended) The method of Claim 15, wherein said site is [to] a tumor.

18. The method of Claim 2, wherein said administering is locally to a site wherein said sensitivity is to be induced.

19. The method of Claim 18, wherein said administering is by injection.

20. (Amended) The method of Claim 18, wherein said site is [to] a tumor.

21. The method of Claim 3, wherein said administering is locally to a site wherein said sensitivity is to be induced.

22. (Amended) The method of Claim 21, wherein said administering is by injection.

23. (Amended) The method of Claim 21, wherein said site is [to] a tumor.

24. The method of Claim 9, wherein said individual is in need of inhibition of cell proliferation, and wherein said administering is locally to a site wherein cell proliferation is to be inhibited.

25. The method of Claim 24, wherein said administering is by injection.

26. (Amended) The method of Claim 24, wherein said site is [to] a tumor.

27. (Amended) The method of Claim 11, wherein said site [has] <u>is</u> a tumor or [wherein a tumor has been removed] where a tumor was previously located prior to removal.

28. The method of Claim 11, wherein said administering is by injection to a tumor

Appendix of Pending Claims

1. (Amended) A method for inhibiting cell proliferation in an individual in vivo comprising administering to said individual a composition comprising a RAD51 antisense molecule thereby inhibiting said cell proliferation.

2. (Amended) A method for inducing sensitivity to radiation in an individual in vivo comprising administering to said individual a composition comprising a RAD51 antisense molecule thereby inducing said sensitivity to radiation.

3. (Amended) A method for inducing sensitivity to a chemotherapeutic agent in an individual in vivo comprising administering to said individual a composition comprising a RAD51 antisense molecule thereby inducing said sensitivity to a chemotherapeutic agent.

4. (Amended) A method for inhibiting the growth of a cancerous cell comprising administering to said cell a composition comprising a RAD51 antisense molecule thereby inhibiting said growth of a cancerous cell.

5. (Amended) A method for inducing sensitivity to radiation in a cancerous cell comprising administering to said cell a composition comprising RAD51 antisense molecule thereby inducing said sensitivity to radiation.

6. (Amended) A method for inducing sensitivity to a chemotherapeutic agent in a cancerous cell comprising administering to said cell a composition comprising RAD51 antisense molecule thereby inducing said sensitivity to a chemotherapeutic agent.

8. The method of Claim 1 further comprising the step of administering radiation.

9. (Amended) A method of prolonging the survival of an individual comprising administration to said individual a RAD51 antisense molecule thereby prolonging said survival.

10. (Amended) A method of treating cancer in an individual comprising administration to said individual a RAD51 antisense molecule thereby treating said cancer in an individual.

11. (Amended) A method according to claim 10 wherein said administration comprises localized delivery of said RAD51 antisense molecule to a cancerous or potentially cancerous site.

12. (Amended) A method according to claim 11 wherein said method further comprises radiation treatment at said site.

13. (Amended) A method according to claim 11 wherein said method further comprises chemotherapeutic treatment of said patient.

15. The method of Claim 1, wherein said administering is locally to a site wherein said cell proliferation is to be inhibited.

16. The method of Claim 15, wherein said administering is by injection.

17. (Amended) The method of Claim 15, wherein said site is a tumor.

18. The method of Claim 2, wherein said administering is locally to a site wherein said sensitivity is to be induced.

19. The method of Claim 18, wherein said administering is by injection.

20. (Amended) The method of Claim 18, wherein said site is a tumor.

21. The method of Claim 3, wherein said administering is locally to a site wherein said sensitivity is to be induced.

22. (Amended) The method of Claim 21, wherein said administering is by injection.

23. (Amended) The method of Claim 21, wherein said site is a tumor.

24. The method of Claim 9, wherein said individual is in need of inhibition of cell proliferation, and wherein said administering is locally to a site wherein cell proliferation is to be inhibited.

25. The method of Claim 24, wherein said administering is by injection.

26. (Amended) The method of Claim 24, wherein said site is a tumor.

27. (Amended) The method of Claim 11, wherein said site is a tumor or where a tumor was previously located prior to removal.

28. The method of Claim 11, wherein said administering is by injection to a tumor